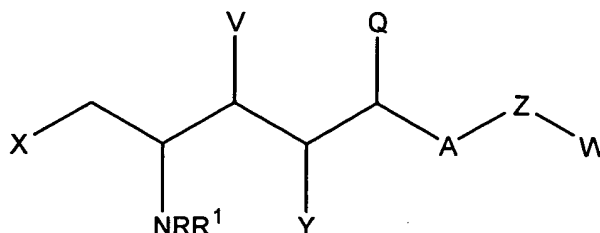


We claim.

1. A sphingolipid derivative of the formula:



10 wherein

A is a spacer group which is  $(CH_2)_m$  where  $m=0-14$ , where any of the hydrogens may be independently replaced by  $R^1$  or X and where any two adjacent carbons may be independently replaced by a  $C_3$ - $C_8$  cycloalkyl group, a 1,2-, 1,3-, or 1,4-disubstituted benzene group, or a 2,3-, 2,4- or 2,5-disubstituted thiophene, furan or pyrrole group;

15 X, Y, V, and Q are independently hydrogen,  $OR^1$ ,  $NR_2$ , CN, alkyl, acyl, carboxylate, and wherein alternatively, V and Y or Y and Q or Q and A can together constitute a double or triple bond;

W = no substituent, H, alkyl, aryl, alkenyl, alkynyl, alkaryl, aralkyl,  $C(O)(CH_2)_nCO_2H$ ,  $C(O)(CH_2)_nCW'_2CO_2H$ , or  $OR^1$  ;

20 W' is selected independently from H, alkyl, aryl,  $(CH_2)_nCO_2H$ ;  $(CH_2)_nCH(CO_2H)CH_2CO_2H$ ; and  $(CH_2)_nCH(CO_2H)CH(CH_2CO_2H)CO_2H$ ;

Z is H, O, NH, NR,  $NHC(O)$ ,  $CO_2$ ,  $C(O)NH$ , or  $C(O)NR$ ;

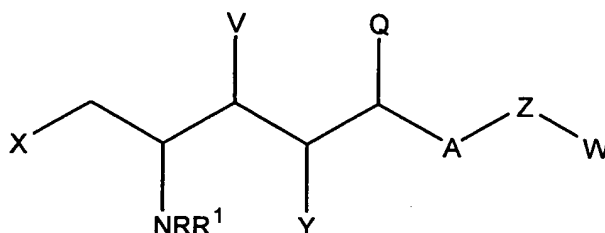
R is selected independently from H, alkyl, acyl, alkenyl, alkynyl, aryl, alkaryl, aralkyl, or heteroaryl;

25  $R^1$  is R or  $R^2$  ;

$R^2$  is phosphate ( $OP(OR_3)$ , wherein at least one R is not hydrogen), b-D-galactoside, N-acetyl-b-D-glucosamine, a-D-mannoside, an organic azo-bond containing moiety that can be reduced by an azoreductase, b-D-cellobiosides, b-D-glucopyranosides, b-D-galactopyranosides, b-D-glucuronides, starch, lactose, raffinose, stachyose, fructooligosaccharides, an amide or ester of b-cyclodextrin, dextran linked via succinate and glutarate, an amino acid or peptide, or a polyamino acid or polypeptide, furanose and pyranose carbohydrates, sulfonate (and esters thereof), phosphocholine, phosphoserine, and phosphoethanolamine;

wherein there is at least one  $R^2$  substituent in the sphingolipid derivative.

2. A sphingolipid derivative of the formula:



wherein

A is alkyl, alkenyl, alkynyl, alkaryl, or aralkyl;

X, Y, V, and Q are independently hydrogen,  $OR^1$ ,  $NR_2$ , OH, CN, alkyl,  $C(O)R$ ,  $OC(O)R$ , and wherein alternatively, V and Y or Y and Q or Q and A can together constitute a double or triple bond;

W is no substituent, H, alkyl, aryl, alkenyl, alkynyl, alkaryl, aralkyl,  $C(O)(CH_2)_nCO_2H$ ,  $C(O)(CH_2)_nCW'_2CO_2H$ , or  $OR^1$ ;

W' is selected independently from H, alkyl, aryl,  $(CH_2)_nCO_2H$ ;  $(CH_2)_nCH(CO_2H)CH_2CO_2H$ ; and  $(CH_2)_nCH(CO_2H)CH(CH_2CO_2H)CO_2H$ ;

Z is H, O, NH, NR, NHC(O), CO<sub>2</sub>, C(O)NH, or C(O)NR;

R is selected independently from H; alkyl, acyl, alkenyl, alkynyl, aryl, alkaryl, aralkyl, or heteroaryl;

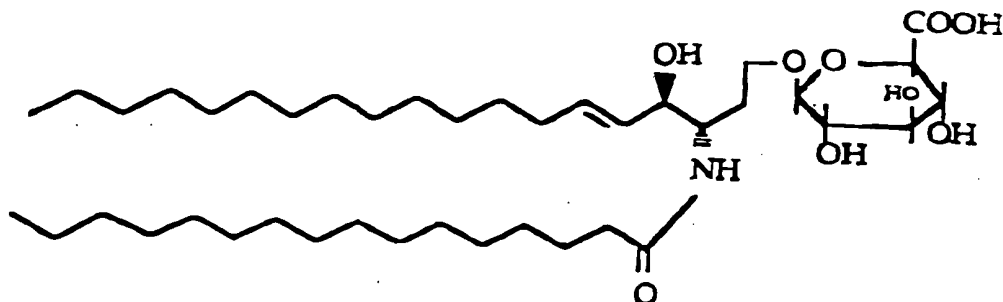
R<sup>1</sup> is R or R<sup>2</sup>;

5 R<sup>2</sup> is a "targeting moiety" that binds to a receptor molecule on the target membrane's surface, selected from the group consisting of steroids, hormones, hormone receptors, cell specific receptors and ligands that bind to cell specific receptors, antibodies, antibody fragments, antigens, T cell receptor fragments, and T cell receptor variable regions;

10 wherein there is at least one R<sup>2</sup> substituent in the sphingolipid derivative.

3. A compound selected from the group consisting of ceramide  $\beta$ -glucuronide; sphinganine  $\beta$ -glucuronide; dihydroceramide  $\beta$ -glucuronide; sphingomyelin  $\beta$ -glucuronide; sphingosine  $\beta$ -glucuronide; ceramide b-D-galactoside; sphinganine b-D-galactoside; dihydroceramide b-D-galactoside; sphingomyelin b-D-galactoside; sphingosine b-D-galactoside; ceramide N-acetyl-b-D-glucosamine; sphinganine N-acetyl-b-D-glucosamine; dihydroceramide N-acetyl-b-D-glucosamine; sphingomyelin N-acetyl-b-D-glucosamine; sphingosine N-acetyl-b-D-glucosamine; ceramide a-D-mannoside; sphinganine a-D-mannoside; dihydroceramide a-D-mannoside; sphingomyelin a-D-mannoside; sphingosine a-D-mannoside; ceramide b-D-cellobioside; sphinganine b-D-cellobioside; dihydroceramide b-D-cellobioside; sphingomyelin b-D-cellobioside; ceramide b-D-glucopyranosides; sphinganine b-D-glucopyranosides; dihydroceramide b-D-glucopyranosides, sphingomyelin b-D-glucopyranosides; sphingosine b-D-glucopyranosides; ceramide b-D-galactopyranosides; sphinganine b-D-galactopyranosides; dihydroceramide b-D-galactopyranosides, sphingomyelin b-D-galactopyranosides; and sphingosine b-D-galactopyranosides.

4. Ceramide  $\beta$ -glucuronide, which has the chemical formula



10 5. The compound of claims 1 or 2, wherein the bond between V and Y, Y and Q or Q and A is double bond.

6. A fumonisin analog to which is directly or indirectly bound an  $R^2$  group selected from the group consisting of phosphate ( $OP(OR_3)$ , (wherein at least one R is not hydrogen), b-D-galactoside, N-acetyl-b-D-glucosamine, a-D-mannoside, an organic azo-bond containing moiety that can be reduced by an azoreductase, b-D-cellobiosides, b-D-glucopyranosides, b-D-galactopyranosides, b-D-glucuronides, resistant starch, lactose, raffinose, stachyose, fructooligosaccharides, an amide or ester of b-cyclodextrin, dextran linked via succinate and glutarate, an amino acid or peptide, or a polyaminoacid or polypeptide, furanose and pyranose carbohydrates, sulfonate (and esters thereof),  
15  
20 phosphocholine, phosphoserine, and phosphoethanolamine.

7. A fumonisin analog to which is directly or indirectly bound an  $R^2$  is a "targeting moiety" that binds to a receptor molecule on the target membrane's surface, selected from the group consisting of steroids, hormones, hormone receptors, cell  
25 specific receptors and ligands that bind to cell specific receptors, antibodies, antibody fragments, antigens, T cell receptor fragments, and T cell receptor variable regions.

8. The compound 1-deoxy-5-hydroxy-sphinganine, wherein at least one R<sup>2</sup> is covalently bound to either hydroxyl group or the amino function of the molecule.

5 9. A method for the treatment of abnormal cell proliferative disorder comprising administering an effective treatment amount of a compound of any one of claims 1-8 to a host in need thereof.

10 10. A method for the treatment of a benign or malignant tumor comprising administering an effective treatment amount of a compound of any one of claims 1-8 to a host in need thereof.

11. The compound of claim 1 or 6 that is cleaved by an appropriate enzyme *in vivo* to release a parent moiety for desired therapy.

15 12. The method of claim 9, wherein the proliferative disorder is selected from the group consisting of colon cancer, intestinal polyps, intestinal tumors, inflammatory bowel diseases, ulcerative colitis and Crohn's disease, necrotizing enterocolitis, ileocectitis, other inflammations of the lower bowel, antibiotic associated colitis, and tumors of the urogenital tract.

20

13. The method of claim 9, wherein the disorder is colon cancer.

25 14. The method of claim 9, wherein the benign tumor is selected from the group consisting of papilloma, adenoma, firoma, chondroma, osteoma, lipoma, hemangioma, lymphangioma, leiomyoma, rhabdomyoma, meningioma, neuroma, ganglioneuroma, nevus, pheochromocytoma, neurilemona, fibroadenoma, teratoma, hydatidiform mole,

granulosa-theca, Brenner tumor, arrhenoblastoma, hilar cell tumor, sex cord mesenchyme, interstitial cell tumor, and thyoma.

15. The method of claim 10, wherein the tumor is selected from the group  
5 consisting of malignant tumors (cancer), prostatic adenocarcinoma, bladder carcinoma, and adenocarcinoma, fibrosarcoma, chondrosarcoma, osteosarcoma, liposarcoma, hemangiosarcoma, lymphangiosarcoma, leiomyosarcoma, rhabdomyosarcoma, myelocytic leukemia, erythroleukemia, multiple myeloma, glioma, meningeal sarcoma, thyoma, cystosarcoma phyllodes, nephroblastoma, teratoma choriocarcinoma, cutaneous  
10 T-cell lymphoma (CTCL), cutaneous tumors primary to the skin, breast and other tumors infiltrating the skin, Kaposi's sarcoma, and premalignant and malignant diseases of mucosal tissues.

16. The method of claim 9, wherein the disorder is selected from the group  
15 consisting of preneoplastic lesions, mycosis fungoides, psoriasis, dermatomyositis, rheumatoid arthritis, viruses, molluscum contagiosum, premalignant and malignant diseases of the female genital tract.

17. A method for triggering the release of cytochrome c in a patient in need  
20 thereof comprising administering an effective amount of a compound selected from the group consisting of sphinganine, dihydroceramide, ceramide, sphingomyelin, ceramide, and sphingosine, or pharmaceutically acceptable salt or an acylated derivative thereof.

18. A method for triggering the release of cytochrome c in a patient in need  
25 thereof comprising administering an effective treatment amount of a compound of any one of claims 1-8.

19. A method for inhibiting protein kinase c in a patient in need thereof, comprising administering an effective treatment amount of a compound of any one of claim 1-8.

5        20. A method for promoting cell differentiation in a patient in need thereof, comprising administering an effective treatment amount of a compound of any one of claims 1-8.

10       21. A method for treating a tumor in a patient comprising administering an effective treatment amount of a compound of claim 6 or 7 in combination with a chemotherapeutic agent.

22. The method of claim 21, wherein the chemotherapeutic agent is doxorubicin.

15       23. A method for the treatment or prevention of a microbial infection caused by a microorganism bearing a sphingolipid receptor which binds to a sphingolipid compound as a means to anchor the microbe and initiate colonization, comprising administering to the host an effective amount of a compound of any one of claim 1-8, or its pharmaceutically acceptable salt, optionally in a pharmaceutically acceptable carrier.

20

24. The method of claim 23, wherein the microbe is a bacteria.

25. The method of claim 23, wherein the microbe is a virus.

25       26. The method of claim 23, wherein the microbe is selected form the group consisting of cholera toxin, verotoxin, Shiga-like toxin 2e, Clostridium botulinum type B

neurotoxin, Escherichia coli, Haemophilus influenzae; Helicobacter pylori; Borrelia burgdorferi, Pseudomonas aeruginosa, Candida albicans, HIV, Sendai virus, and influenza viruses.

5           27. A method for modifying the colonization of microfora that influence colon cancer and other intestinal disorders in a patient, comprising administering an effective treatment amount of a compound of any one of claims 1-8.

10           28. The method of claim 23 wherein the microfora are selected from the group consisting of cholera toxin, verotoxin, Shiga-like toxin 2e, Clostridium botulinum type B neurotoxin, Escherichia coli, Haemophilus influenzae; Helicobacter pylori; Borrelia burgdorferi, Pseudomonas aeruginosa, Candida albicans, HIV, Sendai virus, and influenza viruses.

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